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I DEEPLY feel the honour and the privilege conferred upon me by the President of the Society for the Study of Venereal Diseases by asking me to put before you the ideas of the French School on this subject.

I beg my excellent friend, Dr. Wilfrid Fox, the Officers and Members of the Society to allow me to express here my sincerest thanks, and I crave their indulgence for my

English.

The late Professor Fournier, who remains the master of the French Syphilology, has exposed the principles authorising marriage by syphilitics. He demanded the following conditions:

(1) The absence of symptoms in evolution. Lapse of time being of importance since the last appearance.

(2) That old-standing syphilis should not present any menacing character.

(3) Sufficient treatment.

Not having at his disposal the biological researches which would permit him to appreciate the virulence of syphilis in the absence of symptoms, Fournier had to deal in generalities, and left it to the doctor to decide each case on its own merits as to whether the patient was in a condition to contract marriage.

Owing to the exact research work of to-day (e.g., research on spirochætes, Bordet-Wassermann reactions, etc., and examination of the cerebro-spinal fluid), the solution of the problem can be demonstrated with much greater accuracy.

The question of marriage by syphilitics was approached by the French Society of Dermatology and Syphilis in June, 1920, and a very complete report has been published in the *Bulletin*. However, since that time, new thera-

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peutic methods have been introduced which ought to be seriously considered.

First I shall study the case where syphilis has been contracted *before marriage*, and the conditions which permit the doctor to authorise a syphilitic to marry and raise children. Then I shall say a few words about the precautions to be taken with one who has contracted syphilis *after marriage*.

The frequency of syphilis, the excellent results obtainable with the actual methods of treatment, have rallied in France all syphilologists; and one can say that all consider marriage possible in spite of a syphilitic infection but under the one condition that the disease is properly

treated.

### (I) SYPHILIS CONTRACTED BEFORE MARRIAGE

Syphilis presents dangers to one of the parties who has it, for the infection may cause results later which will diminish or annihilate his physical or intellectual activity; syphilis presents dangers to the other party who is liable to be contaminated and who finds herself then exposed to all the accidents of syphilis, which can be visited upon the children by causing still-birth or death after birth or the appearance of more or less deeply rooted defects which will affect their intelligence or their health. Therefore, from a theoretical standpoint, one should allow a syphilitic to marry only when in possession of absolute proofs against recurrence of the disease, and that he will be incapable of contaminating his partner or transmitting syphilis to his children. Unfortunately an absolute proof of the cure cannot be established either as regards syphilis or tuberculosis or any other chronic infections which are always susceptible to reappear again after long having remained latent.

In Medicine the negative reactions do not indicate an absolute security, and nothing permits us to assume that syphilis has definitely disappeared. The only proof of the complete cure of syphilis which can be considered as indisputable is reinfection, but of course, referring to the cases we are studying here, we are obliged to content ourselves with less substantial arguments. There is no doubt that—and this is indeed a general law of pathology—syphilis, like other infections, has a much better chance of being cured the sooner the treatment is commenced.

We know that during the 15 or 20 days after the appearance of a chancre the B.W. reaction is negative, syphilis remaining locally confined during this stage, nearly all of the spirochætes remaining blocked in the primary sore; the few micro-organisms which, from the first day onwards, cross the ganglionary barrier and invade the organs have not yet caused any reaction in the tissues, remain very vulnerable and the remedies have a great chance of destroying them entirely.

The cure of syphilis is consequently a particularly easy one during the first days in its primary stage, the stage commonly called *the sero-negative primary syphilis* or *the* 

pre-serological period of syphilis.

The cure can be a still easier one when the treatment is commenced before the appearance of chancre, as it has been proved by Dr. Magian in a well-known auto-observation. That this is so I demonstrated in 1918 by instituting a preventive treatment of syphilis in individuals who had had contact with contaminated persons. This fact was pointed out later by Ch. Laurent, Fournier and Guénot, Bodin and many others.

When syphilis has generalised itself, that is when the B.W. reaction is positive, and especially when the secondary symptoms have appeared, we must be more rigorous in our scrutiny of the evidence of cure, for this is the moment when syphilitic infection is easily transmitted.

Great caution must also be exercised during the third stage of the disease, even if infection is more difficult than during the secondary stage.

We shall make a consecutive study of those various cases.

(1) Syphilis treated during Period of Incubation.—When a person has had contact with a syphilitic consort showing contagious symptoms, we consider ourselves authorised to advise the exposed person to undergo a course of preventive treatment. If this treatment is commenced at once and is a very energetic one, there is every chance of preventing the appearance of syphilis. Although favourable results can be obtained with a single injection (Magian), or with three as I have personally observed, it seems reasonable to institute a preventive treatment just as rigorous as if the date of the dangerous contact is remote.

I agree entirely with the ideas of Dr. Ch. Fouquet, who through the Society of Medicine of Paris has published a report on this question. If treatment is commenced the first week after the dangerous contact, one should administer 5 injections of 914 (first of 6 grains, second of 12 grains, and three of 18 grains); if commenced during the second week 8 injections, and if commenced during the third week 10 injections.

Other remedies have been used for the preventive cure of syphilis. Fournier and Guénot have used Stovarsol (Acid-Oxy-Amino-Phenyl-Arsenic). Clément Simon has used Tréparsol (formyl derivative of Acid-Oxy-Amino-Phenyl-Arsenic). These two remedies, which belong to the group of arsinic acids, have the advantage that they can be taken in the form of tablets, 4 tablets of 5 grains a day at meals, dissolved in a little water. This to be continued 4 days in succession, followed by a rest of 3 days in order to allow the excretion of the medica-This cure is to be continued for 8 to 10 weeks. The results have been good, but less reliable than those obtained with 914; and cases have been pointed out where syphilis has broken out, in spite of a preventive treatment, after a much longer incubation than usually is the case. In using this process, the patient in question should be put under a clinical and serological observation for a year after the preventive treatment is finished. If then everything remains normal, marriage may be allowed.

(2) Treatment during the Pre-serological Period.— Should the practitioner find an unquestionable primary sore, the serum, however, still producing a complete negative B.W. reaction, there is hope of obtaining a permanent sterilisation of syphilis in a relatively short time. This pre-serological period does not last more than 20 days at a maximum.

After this the reaction becomes rapidly positive, except in a few extraordinary cases where the reaction is negative even during the secondary period (one or two cases in a hundred at a maximum). The negative reaction has therefore only its entire value during the first 20 days of the disease. After this it will be necessary, even if the reaction is negative, to institute a treatment as rigorous as if the reaction had been positive.

It sometimes happens that treatment is commenced

just at the moment when the B.W. reaction is on the turning point to become positive. If one repeats the blood tests during the course of the treatment, one will notice that the reaction, first negative, turns more or less positive, then negative again as treatment is continued. This transient modification, which Tzanck has called "le crochet positif de la courbe sérologique," shows that the spirochætes have succeeded in crossing the ganglionary barrier and that treatment must be more rigorous than if the reaction had always remained negative.

This also shows the necessity of attempting by a succession of reactions, made weekly during the first series of injections, to see if the positive turn does not take place.

The treatment in these cases must be one that acts quickly, and the French School has entirely agreed upon the intravenous injections of 914. Most of us even think, agreeing with the opinion of Queyrat, that the graduation of doses must be a more rapid one than in the case where syphilis is already generalised, and that one has a better chance in realising the entire sterilisation of the infection by rapidly increasing the doses.

The intravenous injections of compounds of the type 914 should be commenced with small doses (3 grains) in order to sound the susceptibility of the patient; but with the second, which can be administered 3 days after the first, one must attain to the dose of 9 grains; the third injection given 5 days later will be 15 grains, followed by 5 other injections of 18 grains at weekly intervals. The B.W. test is to be carried out during the course of the treatment and also at the end of the series.

After a three weeks' rest, a new B.W. test, followed by a second series of 8 to 10 intravenous injections of 914 (beginning with a 6-grain dose and to be increased by 3 grains each time), should be carried out.

Many are of the opinion that a third and fourth series of intravenous injections of arsenobenzol would be useful. Personally I then prefer to make use of insoluble bismuth preparations, such as iodobismuth of quinine or hydroxide of bismuth in oily suspension, for these preparations, which are less dangerous than the arsenobenzols, have also the advantage of being excreted more slowly and of having a more durable effect.

Two series of 12 to 15 bi-weekly injections of insoluble

bismuth preparations, iodobismuth of quinine, hydroxide of bismuth, etc., each series separated by intervals of 4 to 5 weeks, shall be administered to the patient.

If the reactions obtained between these series continue to be completely negative, then the patient can be put under observation without continuing the treatment.

The B.W. reactions should be repeated at least every two months, and, if they do not vary within a year, most of the French syphilologists consider them as permanently negative. Vernes even states that the negative reaction which has maintained itself for eight months in the absence of any treatment will not vary any more.

To sum up: When syphilis is attacked in the preserological stage, the use of the intravenous injections of arsenobenzol seems to be preferable; the first series should be administered rapidly. The second series should commence 3 weeks after the last injection of the first series. This one is to be followed by a third or two series of insoluble bismuth injections.

The total duration of this treatment to be about 10 to 12 months. After this time an observation period from 8 to 12 months is necessary.

If, after this time, the B.W. reaction remains negative, it would be well to employ a provocative injection according to the method of Milian by injecting 6 to 9 grains of 914 and again to examine the blood 8 or 12 days after the injection.

The result being negative, the lumbar puncture should be made to ascertain if the cerebro-spinal fluid is normal, and if so, the patient may be allowed to marry, 18 months to 2 years being the minimum time which shall have elapsed since the commencement of the treatment.

(3) Treatment commenced after the Appearance of the Positive Reaction.—When the positive reaction has appeared, one can be sure that the syphilitic virus has completely affected the whole organism. If this generalisation is recent, that is to say, if the patient is still in the primary stage, the cure shall be easier obtained than if the secondary symptoms have already made their appearance. In fact when the secondary symptoms manifest themselves in a virulent attack syphilitic infection seems to have reached its height, and it is then that the B.W. reaction shows itself most decidedly positive. But even if the patient has cutaneous, mucous or visceral

lesions, they are almost always curable and, once cured, are no obstacle to marriage.

In these cases the treatment used should aim at the same result: e.g., the production of a totally negative B.W. reaction, the rendering of this reaction permanently negative, and attainment of the evidence by a lumbar puncture that the nerve centres have not been touched. Which is here the treatment to be indorsed? We do not have, as during the sero-negative period, to act with extreme rapidity, and can therefore avoid the rapidly following series of injections which are always liable to harm the patient.

Almost all the French syphilologists put the 914 injections in the first place. Some, like Milian, Marcel Pinard, advise exclusively the intravenous injections, others follow the example of Leonard, admitting the administration of intramuscular injection.

Whilst I agree with the intravenous injections when attacking syphilis in its sero-negative stage and when necessity requires the rapid attaining of strong doses in order to achieve success, I frequently have recourse to the intramuscular injections of 914 when attacking syphilis in the primary stage after the appearance of the

positive reaction, or in the secondary stage.

One should not forget that the question of doses is of great importance as regards the efficacy of the treatment, and I only consider the intramuscular injections effective if one obtains doses equal to those administered by the intravenous method. But if 914 injected into the veins is generally well taken, it is not the same when used as intramuscular injection, therefore one is obliged to resort to the injections of sulfarsenol or sulfotreparsenan, which is less painful than 914. However when one reaches doses of 12 to 15 grains a pain lasting at least 2 days is caused, entailing often a passing inflammation of the muscles of the buttocks, which renders the continuance of the treatment difficult. With patients who do not support the intravenous injections of 914, I frequently use the intramuscular injections of sulfotreparsenan or sulfarsenol, alternating with insoluble bismuth injections, which allow the intramuscular injections or arsenobenzol to be limited to doses of about 12 grains, which cause a very supportable pain. I therefore give once a week an intramuscular injection of sulfarsenol in doses following

the same progress as those of 914 used in intravenous injections, and 3 days after I give an intramuscular injection of bismuth (hydroxide of bismuth or iodobismuth of quinine). This method has the advantage of acting rapidly on the syphilitic lesions on account of the arsenic and of giving a durable effect due to the injection of bismuth which is eliminated much more slowly than the arsenical injection.

Besides, one must remember that if one does not personally apply the treatment, and if the injections have to be made by a practitioner who is not a specialist and who has always a tendency to reduce the doses of arsenical injections in order to avoid accidents, and if one does not combine the arsenobenzols with a more tenacious remedy and of a much slower rate of elimination, the effect on the syphilitic infection remains insufficient.

The injections of bismuth can be used without any arsenic, but if one employs the insoluble preparations which are the best tolerated, one may, in the course of the treatment, see new symptoms manifesting themselves. Clément Simon has observed, in patients treated with insoluble bismuth during the secondary stage, a syphilitic meningitis and a syphilitic optical atrophy. These symptoms can be explained in two ways: either the patient treated resisted the bismuth injections, or the insoluble injections which had been administered acted too slowly and before becoming effective allowed the appearance of new specific localisations. In either event the danger can be avoided by combining arsenic with bismuth.

Whatever may be the method employed, the first care of the practitioner ought to be to obtain from the patient a negative B.W. reaction.

In order to obtain this result, two and sometimes more series are necessary. The treatment must be continued regularly until this result is attained, and there ought to be an interval of only 3 to 4 weeks between the series of injections in order to avoid any recurrence of infection.

If the B.W. and the Hecht reactions be absolutely negative, it will still be necessary to administer to the patient at least two series of injections to make sure of the result. At this time it will be possible to use injections of the insoluble bismuth, there being no longer fear of the appearance of unforeseen syphilitic symptoms. The

blood tests should be taken at the beginning of each series of injections.

Regular treatment should be continued for some time, even if the tests after 2 or 3 series are negative. Treatment for 18 months is the minimum, and I consider it advisable to continue the series of injections during a year after the tests have become negative. As long as the results of the tests are still positive, I use injections of 914 alone, or combined with bismuthal injections. according to the method explained above. When the tests give negative results, I apply during a year a treatment of a series of injections of insoluble bismuth (iodobismuth or hydroxide), at intervals of 4 to 6 weeks. Others continue the treatment further without taking into consideration the more or less rapid negativation of the blood tests. Professor Jeanselme orders a regular treatment from 3 to 4 years, Cl. Simon a treatment of 2 years.

The examination of the cerebro-spinal fluid is done at the moment of suspension of the treatment in order to commence the observation period. If the fluid is normal, treatment is suspended and every two months a blood test is taken. If everything remains normal during 12 to 18 months as it is indicated further above, one gives a provocative injection prior to the B.W. reaction and a new lumbar puncture. If all the tests are negative, marriage shall be authorised, but there must be a minimum lapse of time of two and a half years from the commencement of the treatment.

- (4) Syphilis treated in the Tertiary Stage.—Several cases have to be considered, according to the existence or non-existence of actual lesions.
- (A) There are no lesions, the blood tests are negative, the cerebro-spinal fluid is normal. A provocative injection is employed; if the W.R. is negative and the patient has not shown any lesions for at least two years, marriage can be authorised after a safety treatment of a few months with arsenic-bismuth or bismuth exclusively.
- (B) There are no lesions, but the serum reaction of the blood is more or less positive and the cerebro-spinal fluid is normal. I would infer that in the late stage the B.W. reaction is often difficult to modify. The alternate treatment with arsenobenzol and bismuth is here very much recommended. If the results are insufficient one could

try the arsenical acids (Acetylarsan, Stovarsol and Tréparsol).

Once negative results are obtained, treatment must be continued for several months consisting of two or three supplementary series of injections; the insoluble bismuth preparations being particularly recommended. After this the patient is put under serological observation for 8 to 12 months and then provocative injection is given and lumbar puncture is made, and if the results remain negative marriage is allowed.

(C) Irreducible reactions. It happens occasionally that it seems hopeless to convert a positive B.W. reaction to a negative. These cases must be treated in a particularly energetic manner, for it happens often that syphilis of irreducible resistance is the cause of very grave nervous

troubles (Galliot).

The examination of the cerebro-spinal fluid is here of first importance. If the fluid is not normal, marriage must be forbidden. A number of practitioners however forbid marriage when the cerebro-spinal fluid is normal (Professor Jeanselme, Galliot); others allow marriage after a treatment lasting several years, but advise the patient to take a safety treatment at least twice a year and also have the wife treated when in a pregnant condition (Cl. Simon).

(D) The cerebro-spinal fluid is impaired. It is impossible to authorise marriage as long as the fluid has not become normal. These modifications are slow, and lumbar punctures must not be made too frequently. A new lumbar puncture could be made a year after the first one, and if the result is still positive, two years should elapse before practising another one. After everything has reached its normal state an observation period of at least 2 years is indispensable. One can readily see that the treatment and the subsequent period of observation postpone marriage to a far off date.

(E) There exist cutaneous and mucous lesions. This condition has to be treated like secondary syphilis, that is to say the patient has to be treated very rigorously in order to do away with the actual lesions and to render the B.W. completely negative. This is to be followed by at least 3 series of injections in order to obtain a permanent result, after this the patient should be put under observation for a year and then provocative injection and

lumbar puncture should be made. Marriage may be authorised when the results of all these researches remain

negative.

(F) There exist visceral and nervous symptoms. If the symptoms are really curable the same treatment applies as to the cutaneous or mucous symptoms; but if it is a question of symptoms of which absolute cure cannot be obtained, it is necessary to forbid marriage. For instance Aortitis, Angina Pectoris, Tabes, diminish too considerably the physical value of an individual to allow him to get married. Any fear of progressive genital paralysis obliges one to forbid the marriage. The practitioner should make the patient clearly understand that he should abandon any project of matrimony, but should give him hope of being able to marry later on after the symptoms have been entirely cured. In avoiding discouraging the patient completely one obtains a better chance of continuing the treatment energetically.

Summing up: One can safely say that if syphilis has not exhibited any irremediable symptoms, the conduct of the practitioner should be based on the following

principles:

(I) To cure the actual symptoms.

(2) To obtain negative results from the biological tests of the blood and of the cerebro-spinal fluid.

(3) To continue the treatment long enough to avoid relapse in the symptoms and in the results of the tests.

(4) To put the patient under observation in taking

B.W. tests at regular intervals.

(5) To make certain by giving provocative injections and carrying out examination of the cerebrospinal fluid that all has remained normal.

Some important considerations have to be added:

(I) In spite of all precautions, it may happen that syphilis is transmitted to the children. I have recently observed this fact in a properly treated syphilitic who married after an interruption of treatment of 5 years. To remove as much as possible the contamination of wife and children most of the French syphilologists, in accordance with the opinion of the late Professor Fournier, advise the institution of a rigorous treatment during the weeks preceding marriage. This treatment, which Four-

nier calls "The treatment of the father of the family," is designed to put the husband or wife attacked with old-standing syphilis in the best condition for the procreation of a child, which often occurs in the first weeks following marriage. It is easy to make the individual to understand that there are no actual proofs of the cure of syphilis and that it would be safe for him as well as for his wife and the children who are to be born to undergo a safety treatment from time to time.

(2) The precaution to be taken must be much greater with a woman than with a man.

When a woman has been attacked by syphilis, in spite of negative reactions for years and a normal lumbar puncture, we see too often the result in the shape of abortions or children born infected with hereditary syphilis. It is therefore indispensable, when the wife has been infected with syphilis, to make her take a treatment during pregnancy. For those only whose cure dates far back (eight years according to Gougerot) this precaution can be omitted, but the children should always be watched carefully in order to institute treatment of them and of the mother should the slightest sign of hereditary syphilis be noticed.

(3) If the husband has been infected, one may, as a number of specialists demand, treat the wife during the time of her first pregnancy. To-day we have at our disposal powerful remedies (Stovarsol and especially Tréparsol) which can be administered by the mouth as a disguised treatment for women during their pregnancy.

This precaution is the more justified as we do not know very well the conditions in which syphilis is transmitted

from the parents to the child.

If it is the mother who is infected, we know that the spirochætes invade the placenta (as demonstrated by Levaditi) and contaminate the ovum through the blood-stream.

If it is the father who is infected we know much less about the transmission of the disease. Fournier and Diday believed that the father could infect directly the child ("spermatical infection"), and that the child subsequently contaminates his mother through the maternal and feetal circulations.

Marcel Pinard, who has shown that the sperm of secondary syphilitics could contain spirochætes during

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the secondary period, is of the same opinion. But others, like Augagneur and Carle, think that syphilis cannot be transmitted to the child by the father if the mother has not first been infected. I agree with this, though declaring that the proof of this conjugal contamination is often very difficult and comptimes impossible to obtain

difficult and sometimes impossible to obtain.

There is no doubt that men infected with old-standing syphilis, even perhaps hereditary syphilis, are liable to contaminate their wives, and it is sometimes impossible to find in women contaminated thus any chancre or secondary sores. Often the B.W. reaction proves that the wife has been contaminated, but this proof may fail, and we find instances of the wives of syphilitics who cannot bring their pregnancy to completion, though they have never had any specific symptoms and their B.W. reaction is negative.

Here is an example which I have personally observed.

A man afflicted since childhood with a chronic running of his ear. He marries at about twenty-five years of age and after his marriage an ear specialist has the idea to try an anti-syphilitic treatment. This treatment healed completely his running ear and proved that in this case it was a question of a symptom of syphilis contracted in

his childhood or perhaps of hereditary syphilis.

The wife of this patient became pregnant several times but miscarriages took place. She came with her husband to consult me. Both had a slightly positive B.W. reaction. I applied a rigorous treatment to the wife and two new pregnancies resulted in the birth of two healthy children. In spite of the absence of any symptoms in the wife, it seems that she had been directly contaminated by her husband, although any primary symptoms had escaped observation. The husband could not have contaminated directly the child, because there has never been any spirochætes found in the sperm of old-standing syphilitics.

In the secondary stage the direct transmission by the husband to the wife is still more likely. This brings me to think that in order to have a hereditary syphilitic child,

contamination by the mother is a sine qua non.

I must say a word as regards the treatment of the expectant mother. If this treatment is necessary for one of the reasons mentioned above, the treatment with arsenobenzol given by intravenous or intramuscular

injections seems to show the better results. Although the insoluble bismuth injections have given favourable results (Mme. Cabouat, Galliot) some failures have been noted (Bizard), probably because this treatment acts too slowly.

Personally, in treating pregnant women, I use an alternate treatment consisting of a series of 914 injections, with intervals of 6 weeks during which I administer bi-weekly injections of insoluble bismuth. Thus 2 series of 10 injections of 914 are administered with increasing dosage, followed immediately by 12 bismuthal injections. This treatment lasts 8 months and is stopped about 3 weeks before confinement.

One can administer alternate 914 and bismuth injections, leaving between each of the mixed series an interval of 3 to 4 weeks.

With nine women who were unable to carry a single pregnancy to completion, in 8 cases I have obtained the birth of healthy children by this mixed method (series of 914 injections alternating with series of bismuthal injections). In one case the child, although born healthy in appearance, died at the end of 6 weeks in a fit of convulsions. The father of this child was healthy, but the mother presented all the stigmata of hereditary syphilis and proved to us how much more dangerous the maternal is than the paternal infection.

# (2) Syphilis contracted after Marriage

Having finished with this long statement, I shall only say a word in regard to the case where syphilis is contracted by one of the parties after marriage.

If syphilis is contracted by the husband, this being the most frequent case, it will be necessary to have the wife follow a preventive treatment, as there might be some risks of contamination. This treatment should be given with arsenobenzol as per indications given above (see "Syphilis treated during Period of Incubation").

The bi-weekly injections of acetylarsan can be substituted for arsenobenzol injections, but are less effective. Stovarsol or Tréparsol can also be used, and they have the advantage that they can be administered by the mouth, but the results are less regular than those obtained with arsenical injections.

The precautions and treatment explained in the foregoing should be imposed upon the husband before allowing him to run the risk of procreation. These counsels unfortunately often go unheeded. The husband wishing to hide his misfortune, frequently contaminates his wife.

If the wife contracts syphilis, it is easier to have her undergo a prolonged medical observation and have her avoid pregnancy during the time while there is a chance of transmitting syphilis to the child. One can practically say that if the wife has contracted syphilis it will be indispensable to administer regularly a specific treament at least during pregnancy. Once the child is born, some precautions are indispensable to make sure that it has really escaped infection. The placenta should be examined, remembering that its normal weight should be approximately one-sixth of the child's weight; the syphilitic placenta reaches often one-fourth and even one-third of the child's weight, but is sometimes in appearance and in weight quite normal.

It would be well to take a B.W. and a Hecht blood test of the vascular organ, but this blood is sometimes non-reactive. It will therefore be useful to verify the results in taking several reactions of the child's blood, for the biological tests become often positive only after a few weeks

Finally the child's growth should be carefully watched and if any symptom of hereditary syphilis takes place the baby should be treated in an energetic and prolonged way.